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Refining the erythrocytosis diagnostic pathway: an audit of current practice compared to new BSH guidelines

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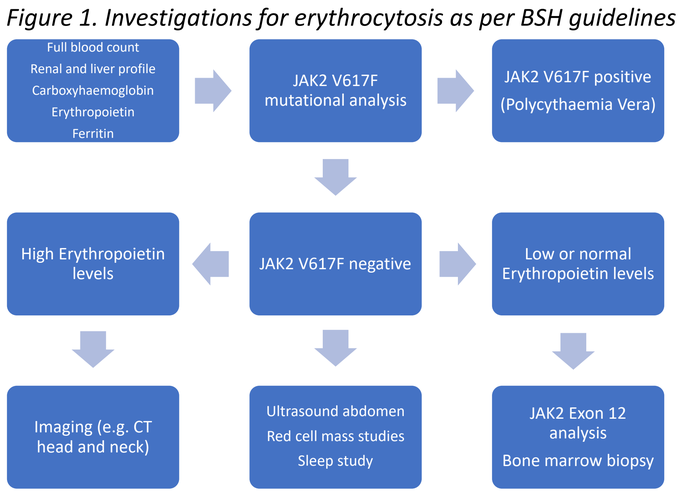
INTRODUCTION

- British Society for Haematology (BSH) updated their guidelines for the diagnosis of erythrocytosis[1] in 2019; this sets out the initial and subsequent investigations recommended for patients with persistent erythrocytosis (haematocrit >0.48 in females and >0.52 in males) as shown below (**figure 1**).
- The guidelines recommend the use of next generation sequencing (NGS) analysis of genes implicated in erythrocytosis for patients who have no cause identified despite the below investigations and are thought to have a possible congenital cause.

Figure 1. Investigations for erythrocytosis as per BSH guidelines



AIMS

- To review current practice in a single tertiary centre in the investigation of erythrocytosis compared to 2019 BSH guidelines recommendations.
- To evaluate whether patients are being appropriately investigated with results reviewed prior to NGS gene panels being requested.

METHOD

- 71 patients with JAK2 V617F negative erythrocytosis who had a NGS red cell gene panel (RCP) sent between April 2016 and January 2019 at our centre were identified.
- Only patients directly referred from primary care to our centre were included. Patients who had previously been investigated for erythrocytosis were excluded.
- Clinical records and laboratory data were retrospectively reviewed to identify patient demographics, medical history and any investigations requested prior to RCP.
- Results of RCP were also reviewed - positive results were classified as either class 3 (variant of unknown significance (VUS)) or class 4 or 5 (pathogenic).

RESULTS

- **26 patients** were included in the review who had been directly referred to our centre from primary care for investigation of erythrocytosis and had a RCP requested as part of their work-up.
- The majority of these patients underwent initial investigations as advised by BSH guidelines as shown in **Figure 2. 100%** of patients had a full blood count, erythropoietin level and JAK2 V617F mutation analysis. Around **75%** of patients had a renal and liver profile, carboxyhaemoglobin and ferritin levels requested.

Table 1. Patient characteristics

Variables	n = 26
Age at presentation, *years*, median (range)	49 (19 – 78)
Haematocrit at presentation, median (range)	
Total	0.517 (0.459 – 0.619)
Male	0.54 (0.48 – 0.619)
Female	0.482 (0.459 – 0.55)
Sex, *female*, n (%)	10 (38.5%)
Current smoker, n (%)	7 (26.9%)
History of arterial or venous thrombosis, n (%)	3 (11.5%)

Figure 2. Frequency of initial investigations requested

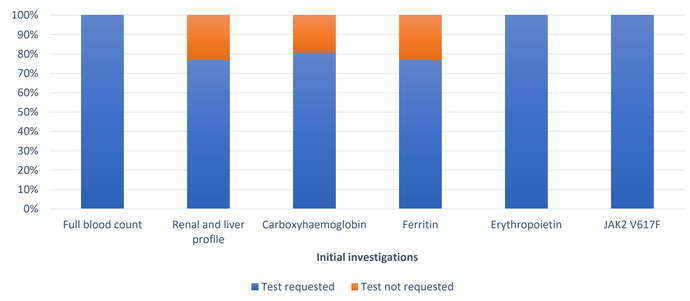
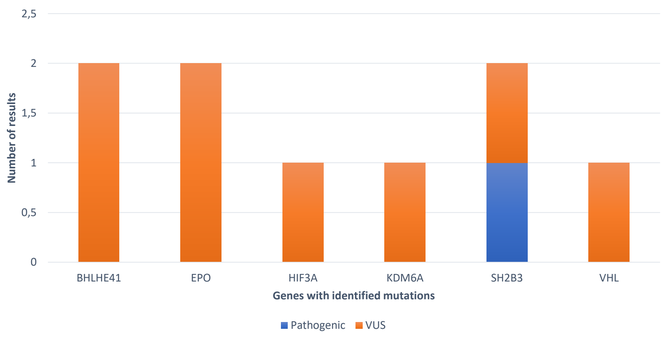


Figure 3. RCP results



- The number and percentage of patients undergoing both initial and further investigations with the results of these are listed in **table 2.**
- **Figure 3** shows results of RCP for these patients – 1 patient had a positive result (3.8%) and 7 patients had at least one VUS (26.9%).

Table 2. Investigation results

Investigations	Results, n (%)
Erythropoietin, n = 26 (100%)	
Low (<5 IU/L)	5 (19.2%)
Normal (5 – 25 IU/L)	21 (80.8%)
High (>25 IU/L)	0 (0%)
Carboxyhaemoglobin, n = 21 (80.8%)	
High (>2.5%)	9 (42.9%)
Normal (<2.5%)	12 (57.1%)
Abdominal imaging, CT/US, n = 21 (80.8%)	
No abnormalities detected	16 (76.2%)
Fatty liver	4 (19.0%)
Splenomegaly	1 (4.8%)
Red cell mass study, n = 16 (61.5%)	
>125% predicted	9 (56.3%)
=<125% predicted	7 (43.7%)
Sleep study, n = 8 (30.8%)	
Mild OSA	2 (25%)
Normal	6 (75%)
JAK2 Exon 12 mutational analysis, n = 23 (88.5%)	
Negative	23 (100%)
Bone marrow biopsy, n = 14 (53.8%)	
No evidence of MPN	14 (100%)
Head+/-neck imaging, CT/MRI, n = 2 (7.8%)	
No abnormalities detected	2 (100%)

CONCLUSIONS

- The patients included in this review were all referred prior to the BSH guidelines being introduced. Despite this, the initial investigations as per the guidelines were still requested for the majority of patients.
- There are still some improvements to be made in order to achieve 100% of all patients undergoing appropriate initial and further investigations.
- The results of the investigations for a significant number of patients suggested possible secondary acquired causes for their erythrocytosis (e.g. smoker or OSA) and therefore, requesting of a RCP may not have been appropriate.
- Ensuring the initial investigations are diligently requested and reviewed prior to RCP may allow this expensive resource to be used more appropriately and improve the positive outcome rate.

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CONTACT INFORMATION

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REFERENCES

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